Complete Summary

GUIDELINE TITLE

Fludarabine monotherapy for the first-line treatment of chronic lymphocytic leukaemia.

BIBLIOGRAPHIC SOURCE(S)

National Institute for Health and Clinical Excellence (NICE). Fludarabine monotherapy for the first-line treatment of chronic lymphocytic leukaemia. London (UK): National Institute for Health and Clinical Excellence (NICE); 2007 Feb. 24 p. (Technology appraisal guidance; no. 119).

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE
METHODOLOGY - including Rating Scheme and Cost Analysis
RECOMMENDATIONS
EVIDENCE SUPPORTING THE RECOMMENDATIONS
BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS
QUALIFYING STATEMENTS
IMPLEMENTATION OF THE GUIDELINE
INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES
IDENTIFYING INFORMATION AND AVAILABILITY
DISCLAIMER

SCOPE

DISEASE/CONDITION(S)

Chronic lymphocytic leukemia (CLL)

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Treatment

CLINICAL SPECIALTY

Hematology
Internal Medicine
Oncology

INTENDED USERS

Advanced Practice Nurses
Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To evaluate the clinical effectiveness and cost-effectiveness of fludarabine monotherapy for the first-line treatment of chronic lymphocytic leukemia

TARGET POPULATION

Patients with chronic lymphocytic leukemia (CLL)

INTERVENTIONS AND PRACTICES CONSIDERED

Fludarabine (Fludara) monotherapy for the first-line treatment of chronic lymphocytic leukemia was considered but not recommended

MAJOR OUTCOMES CONSIDERED

- Clinical effectiveness
    - Progression-free survival
    - Health-related quality of life
    - Treatment response rates
    - Incidence of adverse events
    - Overall survival
- Cost-effectiveness

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Clinical Excellence (NICE) commissioned an independent academic centre to perform an assessment of the manufacturer's submission on the technology considered in this appraisal and prepare an Evidence Review Group (ERG) report. The ERG report for this technology appraisal was prepared by the Centre for Health Economics, University of York and National Health Service (NHS)

Northern and Yorkshire Regional Drug and Therapeutics Centre (see the "Availability of Companion Documents" field).

Clinical Effectiveness

Search Strategy

A systematic literature search was undertaken by the ERG to verify the completeness of the methodology used by the manufacturer to retrieve relevant clinical studies presented in the submission.

Inclusion Criteria

Participants: Chronic Lymphocytic Leukaemia

Interventions: Fludarabine

Comparator: Any

Outcomes: No restrictions applied (outcomes included: overall survival, progression-free survival, overall response, complete response, partial response, adverse drug reactions, and quality of life)

Design: Randomised controlled trial (RCT)

Exclusion Criteria

Participants: Previously treated patients

Intervention: None

Refer to Appendix 2 of the ERG Report (see the "Availability of Companion Documents" field) for information on study selection, databases, and terms searched.

Relevant Ongoing Studies

The following databases were searched for current research: Current Controlled Trials register (searched across multiple registers, including, ISRCTN, MRC NHS, and the National Institutes of Health registers), IFPMA, proceedings of the American Society for Clinical Oncology, National Research Register and the National Cancer Institute, British Society for Haematology, Leukaemia Research Fund, Scirus and a general web search using Google.

Other than more complete and fully published results of the studies included in the manufacturer's submission (principally CLL4 & CLL5), two studies were identified as relevant ongoing trials that are likely to provide significant additional evidence within the next 6 to 12 months.

NUMBER OF SOURCE DOCUMENTS

Clinical Effectiveness

Manufacturer submitted 7 studies.

Two ongoing studies were identified by the Evidence Review Group (ERG).

Cost-Effectiveness

Two papers were identified in both the manufacturer's submission and the ERG searches which reported on the cost-effectiveness of fludarabine monotherapy in comparison to chlorambucil in the management of chronic lymphocytic leukaemia (CLL) in previously untreated patients.

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Clinical Excellence (NICE) commissioned an independent academic centre to perform an assessment of the manufacturer's submission on the technology considered in this appraisal and prepare an Evidence Review Group (ERG) report. The ERG report for this technology appraisal was prepared by the Centre for Health Economics, University of York and National Health Service (NHS) Northern and Yorkshire Regional Drug and Therapeutics Centre (see the "Availability of Companion Documents" field).

Clinical Effectiveness

Submission Trial Analysis

All studies included in the clinical evidence section of the Schering Health Care Ltd (SHC) submission were subjected to a detailed critical appraisal. The resultant appraisals were then compared to the data presented in the submission.

Refer to Section 4.2 of the ERG Report (see the "Availability of Companion Documents" field) for detailed discussion of the included trials.

Meta-Analyses

Of the seven studies included in the submission, only two were fully published and the remaining five studies were available in abstract form only (Refer to Table 4.1 in the ERG Report [see the "Availability of Companion Documents" field]). These abstracts are unlikely to have been subject to peer-review and there are insufficient data in terms of the methods and results presented to allow for their inclusion in a robust meta-analysis. Of the two fully published studies one compares fludarabine (F) with fludarabine plus cyclophosphamide (FC) whilst the other compares F with chlorambucil (Chl). Therefore, pooling of data would not add further insight to the decision problem.

Economic Evaluation

Sensitivity Analyses

The manufacturer's submission includes simple one-way deterministic survival analysis, probabilistic sensitivity analysis, and scenario analyses.

Model Validation

The submission reports that the structure and key assumptions in the model have been validated by two experts in the treatment of chronic lymphocytic leukaemia (CLL). They also report that numeric values in the model have been checked by an experienced modeller not involved in the construction of the model or the subsequent analyses.

Critique of Manufacturer's Economic Model

The ERG has considered the methods applied in the manufacturer's economic evaluation in the context of the critical appraisal questions listed in Table 5.2 of the ERG Report (see the "Availability of Companion Documents" field) which are drawn from common checklists for economic evaluation methods.

Additional Sensitivity Analyses Undertaken by the ERG

A key assumption made in the manufacturer's submission was that the re-treatment response rate for FC was the same as the initial treatment response rate. This assumption was made on the basis that no other evidence was identified to inform this parameter estimate. While such an approach may be considered justifiable (in the absence of contradictory evidence from the literature), it does appear a strong assumption given that the evidence for the re-treatment response rates for F and Chl reported in the literature are both lower than the estimates used for first-line treatment. The ERG was also concerned that the choice of values used in the sensitivity analysis undertaken in the submission for FC was not sufficiently rigorous to test the robustness of the model results, since it was based on the 95% confidence interval from the bootstrap of the initial treatment rate. The ERG has varied the potential probability of response to re-treatment with FC from 0.1 to 0.9 to determine how sensitive the cost-effectiveness results are to this parameter. The results are provided in Table 6.1 of the Assessment Report (see the "Availability of Companion Documents" field).

The results of the additional sensitivity analysis demonstrate that the re-treatment response rate would have to be significantly lower than that assumed for first-line treatment before this might result in a change to the decision related to the cost-effectiveness of FC. Indeed, the results suggest that the re-treatment response rate would have to fall to somewhere between 0.3 and 0.4 before FC no longer appears cost-effective in comparison to Chl.

Refer to Sections 4, 5, and 6 of the ERG Report (see the "Availability of Companion Documents" field) for additional information on methods used to analyze the evidence.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Considerations

Technology appraisal recommendations are based on a review of clinical and economic evidence.

Technology Appraisal Process

The National Institute for Health and Clinical Excellence (NICE) invites 'consultee' and 'commentator' organisations to take part in the appraisal process. Consultee organisations include national groups representing patients and carers, the bodies representing health professionals, and the manufacturers of the technology under review. Consultees are invited to submit evidence during the appraisal and to comment on the appraisal documents.

Commentator organisations include manufacturers of the products with which the technology is being compared, the National Health Service (NHS) Quality Improvement Scotland and research groups working in the area. They can comment on the evidence and other documents but are not asked to submit evidence themselves.

NICE then commissions an independent academic centre to review published evidence on the technology and prepare an 'assessment report'. Consultees and commentators are invited to comment on the report. The assessment report and the comments on it are then drawn together in a document called the evaluation report.

An independent Appraisal Committee then considers the evaluation report. It holds a meeting where it hears direct, spoken evidence from nominated clinical experts, patients and carers. The Committee uses all the evidence to make its first recommendations, in a document called the 'appraisal consultation document' (ACD). NICE sends all the consultees and commentators a copy of this document and posts it on the NICE website. Further comments are invited from everyone taking part.

When the Committee meets again it considers any comments submitted on the ACD; then it prepares its final recommendations in a document called the 'final appraisal determination' (FAD). This is submitted to NICE for approval.

Consultees have a chance to appeal against the final recommendations in the FAD. If there are no appeals, the final recommendations become the basis of the guidance that NICE issues.

Who is on the Appraisal Committee?

NICE technology appraisal recommendations are prepared by an independent committee. This includes health professionals working in the NHS and people who are familiar with the issues affecting patients and carers. Although the Appraisal Committee seeks the views of organisations representing health professionals, patients, carers, manufacturers and government, its advice is independent of any vested interests.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

The manufacturer's submission contained an economic analysis comparing fludarabine monotherapy, fludarabine plus cyclophosphamide and chlorambucil. Only the economic evidence for fludarabine monotherapy compared with chlorambucil is presented in the original guideline document. The economic analyses were based on a Markov state transition model with a 20-year time horizon. The economic model used patient-level data from the CLL4 trial to inform first-line treatment, with data for second-line and salvage treatments taken from a variety of published sources. The manufacturer submitted revised base-case economic analyses following clarifications requested by the Evidence Review Group (ERG). These showed an incremental cost-effectiveness ratio (ICER) of 26,105 pounds sterling per quality-adjusted life year (QALY) for fludarabine monotherapy compared with chlorambucil.

The ERG assessed the manufacturer's economic model and noted that the main drivers of the ICERs presented were time horizon and rates of response to retreatment with the same chemotherapeutic agent as that used in first-line treatment.

The ICER for fludarabine monotherapy compared with chlorambucil for a 15-year time horizon was 28,178 pounds sterling per QALY. For 10-year and 5-year time horizons the ICERs were 42,516 pounds sterling per QALY and 310,663 pounds sterling per QALY, respectively. The ERG stated that the extrapolation of model data is likely to be central to the validity of the ICERs presented. The ERG also noted that an assumption of constant transition probabilities over time was used within the manufacturer's model. Because patient-level data from the CLL4 trial were available, the ERG stated that this assumption should have been validated using formal survival analysis. It therefore performed a survival analysis using patient-level data from the CLL4 trial, the results of which showed that the

assumption of constant transition probabilities is not supported. However, incorporating the results of the ERG's survival analysis into the economic model would have required a substantial restructuring of the model. Correcting this assumption was expected to increase the ICER for fludarabine monotherapy compared with chlorambucil.

The ERG report noted the way in which retreatment response rates for fludarabine monotherapy and chlorambucil were modelled. For fludarabine monotherapy, the first-line treatment response rate (77%) was taken from the CLL4 study and the retreatment response rate (74%) was taken from the existing literature as presented in the manufacturer's submission. For chlorambucil, the first-line treatment response rate (69%) was taken from the CLL4 study and the retreatment response rate (35%) was taken from the existing literature as presented in the manufacturer's submission. This led to a base-case ICER of 26,105 pounds sterling per QALY for fludarabine monotherapy compared with chlorambucil. Because no retreatment response rates were available from the CLL4 study, and because of the limited evidence available in existing literature, the manufacturer's submission presented a one-way sensitivity analysis in which retreatment response rates were assumed to be the same as first-line treatment response rates for all the treatment arms in the economic model. This resulted in an ICER of 86,770 pounds sterling per QALY for fludarabine monotherapy compared with chlorambucil.

The ERG noted that the manufacturer's submission stated that improved progression-free survival with fludarabine monotherapy was linked to improvements in quality of life in the CLL4 trial. However, the impact of the adverse effects of fludarabine, specifically the potential additional costs related to increased hospitalisations due to infections, was not explored in the manufacturer's economic model. Although the manufacturer's model included sensitivity analysis to assess potential decreases in utilities and quality of life as a result of adverse events, the ERG considered that the omission of the treatment costs of adverse events was likely to have resulted in an underestimation of the ICERs for fludarabine monotherapy compared with chlorambucil.

METHOD OF GUIDELINE VALIDATION

External Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Consultee organizations from the following groups were invited to comment on the draft scope, Assessment Report and the Appraisal Consultation Document (ACD) and were provided with the opportunity to appeal against the Final Appraisal Determination.

- Manufacturer/sponsors
- Professional/specialist and patient/carer groups
- Commentator organisations (without the right of appeal)

In addition, individuals selected from clinical expert and patient advocate nominations from the professional/specialist and patient/carer groups were also invited to comment on the ACD.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

This technology appraisal considers the clinical and cost effectiveness of fludarabine monotherapy only. No recommendations have been made with respect to fludarabine plus cyclophosphamide combination therapy because the current marketing authorisation does not specifically provide a recommendation that fludarabine should be used concurrently with other drugs for the treatment of chronic lymphocytic leukaemia.

Clarification was sought with the Medicines and Healthcare Regulatory Authority (MHRA) on the issue of the inclusion of the combination of fludarabine and cyclophosphamide in the marketing authorisation of fludarabine. In all correspondence received from the MHRA, including that shared with National Institute for Health and Clinical Excellence (NICE) by Schering Health Care Limited, it has been made clear that "the MHRA does not consider that the current marketing authorisations for oral and intravenous (i/v) Fludara (PL/0053/0239 and /0290) specifically provide a recommendation that fludarabine should be used concurrently with other drugs for the treatment of chronic lymphocytic leukaemia."

The MHRA has further clarified that, in general, it would expect a manufacturer or sponsor to request a variation in the marketing authorisation when:

1. The summary of product characteristics (SPC) in general, and specifically the "therapeutic indications" section, does not contain references to the combination therapy and the company wishes to promote the use of combination therapy
2. The use of the combination has implications for the dosage specifications in the "posology and method of administration" section of the SPC

In the case of fludarabine, the SPCs do not contain references to the combination therapy. With reference to the second point, the dosage of fludarabine (i/v 25 mg/m^2 for 3 days and oral 24 mg/m^2 for 5 days) in the evidence base for the combination therapy that was submitted by the manufacturer (the CLL4 trial) is different from the fludarabine dosage specified in its SPCs (i/v 25 mg/m^2 for 5 days and oral 40 mg/m^2 for 5 days).

Fludarabine monotherapy, within its licensed indication, is not recommended for the first-line treatment of chronic lymphocytic leukaemia.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of evidence supporting the recommendations is not specifically stated.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate use of fludarabine for the treatment of chronic lymphocytic leukemia

POTENTIAL HARMS

The most common adverse events associated with fludarabine treatment include anaemia, thrombocytopenia, neutropenia and infections (for example, pneumonia and herpes virus infections).

For full details of side effects and contraindications, see the summary of product characteristics (SPC) available at http://emc.medicines.org.uk/.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

This guidance represents the view of the Institute, which was arrived at after careful consideration of the available evidence. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. The guidance does not, however, override the individual responsibility of healthcare professionals to make appropriate decisions in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

- The Healthcare Commission assesses the performance of National Health Service (NHS) organisations in meeting core and developmental standards set by the Department of Health in "'Standards for better health" issued in July 2004. The Secretary of State has directed that the NHS provides funding and resources for medicines and treatments that have been recommended by National Institute for Health and Clinical Excellence (NICE) technology appraisals normally within 3 months from the date that NICE publishes the guidance. Core standard C5 states that healthcare organisations should ensure they conform to NICE technology appraisals.
- "Healthcare Standards for Wales"' was issued by the Welsh Assembly Government in May 2005 and provides a framework both for self-assessment by healthcare organisations and for external review and investigation by Healthcare Inspectorate Wales. Standard 12a requires healthcare organisations to ensure that patients and service users are provided with effective treatment and care that conforms to NICE technology appraisal guidance. The Assembly Minister for Health and Social Services issued a Direction in October 2003 which requires Local Health Boards and NHS Trusts

to make funding available to enable the implementation of NICE technology appraisal guidance, normally within 3 months.

- NICE has developed tools to help organisations implement this guidance (listed below). These are available on NICE website (http://guidance.nice.org.uk/TA119) (see also the "Availability of Companion Documents" field).
    - A costing statement explaining the resource impact of this guidance.
    - Audit criteria to monitor local practice.

IMPLEMENTATION TOOLS

Audit Criteria/Indicators
Patient Resources
Quick Reference Guides/Physician Guides
Resources

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

National Institute for Health and Clinical Excellence (NICE). Fludarabine monotherapy for the first-line treatment of chronic lymphocytic leukaemia. London (UK): National Institute for Health and Clinical Excellence (NICE); 2007 Feb. 24 p. (Technology appraisal guidance; no. 119).

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2007 Feb

GUIDELINE DEVELOPER(S)

National Institute for Health and Clinical Excellence (NICE) - National Government Agency [Non-U.S.]

SOURCE(S) OF FUNDING

National Institute for Health and Clinical Excellence (NICE)

GUIDELINE COMMITTEE

Appraisal Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Committee Members: Dr Jane Adam, Radiologist, St George's Hospital, London; Professor A E Ades, MRC Senior Scientist, MRC Health Services Research Collaboration, Department of Social Medicine, University of Bristol; Dr Amanda Adler, Consultant Physician, Addenbrooke's Hospital, Cambridge; Dr Tom Aslan, General Practitioner, Stockwell, London; Professor David Barnett (*Chair*) Professor of Clinical Pharmacology, University of Leicester; Mrs Elizabeth Brain, Lay Member; Dr Karl Claxton, Health Economist, University of York; Dr Richard Cookson, Senior Lecturer in Health Economics, School of Medicine Health Policy and Practice, University of East Anglia; Mrs Fiona Duncan, Clinical Nurse Specialist, Anaesthetic Department, Blackpool Victoria Hospital, Blackpool; Dr Paul Ewings, Statistician, Taunton and Somerset NHS Trust, Taunton; Professor John Geddes, Professor of Epidemiological Psychiatry, University of Oxford; Mr John Goulston, Director of Finance, Barts and the London NHS Trust; Ms Linda Hands, Consultant Surgeon, John Radcliffe Hospital; Dr Rowan Hillson, Consultant Physician, Diabeticare, The Hillingdon Hospital; Professor Philip Home (*Vice Chair*) Professor of Diabetes Medicine, University of Newcastle upon Tyne; Dr Terry John, General Practitioner, The Firs, London; Professor Richard Lilford, Professor of Clinical Epidemiology, Department of Public Health and Epidemiology, University of Birmingham; Dr Simon Mitchell, Consultant Neonatal Paediatrician, St Mary's Hospital, Manchester; Dr Alec Miners, Lecturer in Health Economics, London School of Hygiene and Tropical Medicine; Ms Judith Paget, Chief Executive, Caerphilly Local Health Board, Wales; Dr Ann Richardson, Lay Member; Dr Stephen Saltissi, Consultant Cardiologist, Royal Liverpool University Hospital; Mr Mike Spencer, General Manager, Clinical Support Services, Cardiff and Vale NHS Trust; Mr Mike Spencer, General Manager, Clinical Support Services, Cardiff and Vale NHS Trust; Dr Debbie Stephenson, Head of HTA Strategy, Eli Lilly and Company; Professor Andrew Stevens, Professor of Public Health, University of Birmingham; Dr Cathryn Thomas, General Practitioner & Associate Professor, Department of Primary Care & General Practice, University of Birmingham; Simon Thomas, Consultant Physician, General Medicine and Clinical Pharmacology, Newcastle Hospitals NHS Trust; Mr David Thomson, Lay Member; Dr Norman Vetter, Reader, Department of Epidemiology, Statistics and Public Health, College of Medicine, University of Wales, Cardiff; Professor Mary Watkins, Professor of Nursing, University of Plymouth; Dr Paul Watson, Director of Commissioning, East England Strategic Health Authority

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) format from the National Institute for Health and Clinical Excellence (NICE) Web site.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Fludarabine monotherapy for the first-line treatment of chronic lymphocytic leukaemia. Quick reference guide. London (UK): National Institute for Health and Clinical Excellence (NICE); 2007 Feb. 2 p. (Technology appraisal 119). Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site.
- Costing statement: Fludarabine monotherapy for the first-line treatment of chronic lymphocytic leukaemia. London (UK): National Institute for Health and Clinical Excellence (NICE); 2007 Feb. 1 p. (Technology appraisal 119). Available in Portable Document Format (PDF) from the NICE Web site.
- Fludarabine monotherapy for the first-line treatment of chronic lymphocytic leukaemia. Audit criteria. London (UK): National Institute for Health and Clinical Excellence (NICE); 2007 Feb. 8 p. (Technology appraisal 119). Available in Portable Document Format (PDF) from the NICE Web site.
- Fludarabine phosphate for the first-line treatment of chronic lymphocytic leukaemia. Evidence Review Group Report. Centre for Health Economics, University of York, and NHS Northern and Yorkshire Regional Drug and Therapeutics Centre, York, UK. 2006 Oct 17. 118 p. Electronic copies: Available from the NICE Web site.

Print copies: Available from the National Health Service (NHS) Response Line 0870 1555 455. ref: N1203. 11 Strand, London, WC2N 5HR.

PATIENT RESOURCES

The following is available:

- Fludarabine for chronic lymphocytic leukaemia. Understanding NICE guidance - Information for people who use NHS services. London (UK): National Institute for Health and Clinical Excellence (NICE); 2007 Feb. 4 p. (Technology appraisal 119).

Electronic copies: Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site.

Print copies: Available from the NHS Response Line 0870 1555 455. ref: N1204. 11 Strand, London, WC2N 5HR.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC STATUS

This NGC summary was completed by ECRI Institute on August 6, 2007.

The National Institute for Health and Clinical Excellence (NICE) has granted the National Guideline Clearinghouse (NGC) permission to include summaries of their Technology Appraisal guidance with the intention of disseminating and facilitating the implementation of that guidance. NICE has not verified this content to confirm that it accurately reflects the original NICE guidance and therefore no guarantees are given by NICE in this regard. All NICE technology appraisal guidance is prepared in relation to the National Health Service in England and Wales. NICE has not been involved in the development or adaptation of NICE guidance for use in any other country. The full versions of all NICE guidance can be found at www.nice.org.uk.

COPYRIGHT STATEMENT

DISCLAIMER

NGC DISCLAIMER

The National Guideline Clearinghouse™ (NGC) does not develop, produce, approve, or endorse the guidelines represented on this site.

All guidelines summarized by NGC and hosted on our site are produced under the auspices of medical specialty societies, relevant professional associations, public or private organizations, other government agencies, health care organizations or plans, and similar entities.

Guidelines represented on the NGC Web site are submitted by guideline developers, and are screened solely to determine that they meet the NGC Inclusion Criteria which may be found at http://www.guideline.gov/about/inclusion.aspx .

NGC, AHRQ, and its contractor ECRI Institute make no warranties concerning the content or clinical efficacy or effectiveness of the clinical practice guidelines and

related materials represented on this site. Moreover, the views and opinions of developers or authors of guidelines represented on this site do not necessarily state or reflect those of NGC, AHRQ, or its contractor ECRI Institute, and inclusion or hosting of guidelines in NGC may not be used for advertising or commercial endorsement purposes.

Readers with questions regarding guideline content are directed to contact the guideline developer.

Date Modified: 9/15/2008